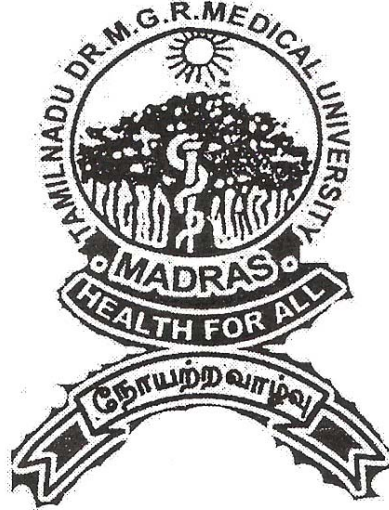


DISSERTATION

**A STUDY ON THE CLINICAL PRESENTATION  
AND THE SENSITIVITY OF FNAC IN THYROID  
NEOPLASMS**

**M.S. DEGREE EXAMINATION  
BRANCH – I  
GENERAL SURGERY**



**THANJAVUR MEDICAL COLLEGE  
THE TAMIL NADU Dr. MGR MEDICAL UNIVERSITY  
CHENNAI**

**SEPTEMBER 2006**

## **ACKNOWLEDGEMENT**

I thank the Almighty without whose help, this work would not have been possible. I am extremely thankful to The Dean, Thanjavur Medical College Hospital for permitting me to conduct this study and to use the materials of the Hospital.

I have great pleasure in expressing my deep sense of gratitude to my unit chief, **Prof. Dr. A. Devakumari**, M.S., Thanjavur Medical College, Thanjavur., for suggesting the topic, providing able guidance and constructive criticism. Her interest, special

guidance, constant encouragement and patience contributed much to the making of this work successfully.

I am very much indebted to **Prof. V. Thirugnanam**, M.S., M.Ch., Head of the Department of surgery, Thanjavur Medical College, Thanjavur for providing all departmental facilities with kind encouragement throughout the period of my work.

I also owe my gratitude to all the unit chiefs of the surgical department of Thanjavur Medical College and **Prof. Dr. Umadevi**, Professor of Pathology, Thanjavur Medical College, Thanjavur without whose valuable material and constant help the completion of this dissertation work would not have been possible.

The kind and valuable criticism of Asst. Surgeons of Thanjavur Medical College, Thanjavur was immensely helpful in completing the dissertation. I thank the medical record section and the library staff for their help.

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## **A STUDY ON THE CLINICAL PRESENTATION AND THE SENSITIVITY OF FNAC IN THYROID NEOPLASMS**

### **INTRODUCTION**

**Thyroid neoplasm includes both benign and malignant tumours arising in the thyroid gland. Although thyroid cancer accounts for only 1% of all cancers (2% in females & 0.5% in males) it is the commonest endocrine tumour that shows a geographic variation in incidence of tumour, type and natural history. Thyroid cancers are heterogenous group of tumours with variable rates of growth, biological aggressiveness, histologic appearance and response to therapy.**

These tumours are rare in children increase in frequency with increase in age. Female to male ratio 2.5 : 1. The autopsy incidence of thyroid carcinoma in United States has been reported to be in range of 0.9% to 13%. It is likely that many thyroid cancers detected in these studies are not clinically significant and do not play a role in the clinical course of the patients. The annual mortality from thyroid cancer in the United States is only 6 per million population or approximately 1050 patients per year. This discrepancy between the incidence and mortality rate presumably reflects the

favorable prognosis for most of the thyroid cancers although these are capable of aggressive behavior with metastatic disease and ultimately death.

In thyroid, Nodules become palpable, if they increase approximately beyond 1 cm in size. In the west 4% of general population has detectable enlargement of thyroid. Although thyroid nodules are common, clinically detectable thyroid cancer is uncommon.

FINE NEEDLE ASPIRATION CYTOLOGY is a very useful first line investigation in case of thyroid nodules BAM FORTH (1966) defined FNAC as “Examination of cells obtained by needle or drill biopsy in solid organs or tissue masses or from the cut surface of such material freshly removed by surgical biopsy”.

In the thyroid swelling the utility of FINE NEEDLE ASPIRATION CYTOLOGY depends upon the accuracy, with which it can predict Neoplasia in thyroid swelling there by providing,

- ❑ The potential for the avoidance of essentially diagnostic surgery in benign conditions
- ❑ For the planning of surgical strategy in case of carcinoma
- ❑ For the avoidance of open biopsy in an advanced carcinoma.

- The FNAC also establishes the physical characteristic of an isolated swelling in that if fluid is obtained from the cysts, if the cyst is abolished and benign then the FNAC is therapeutic.
- A recurrent cyst or residual swelling both of which are suspicious of underlying carcinoma, indications for surgery.

In this dissertation, the main aim of this present study is to report the observations made regarding the clinical presentation and to find out the sensitivity of FNAC in those thyroid neoplasms ultimately proven by Histo Pathological Examination at Thanjavur Medical College Hospital over a period of two years and two months, that is from January 2004 to February 2006.

## **AIMS OF THE STUDY**

- ❑ To study the distribution of the benign and malignant Thyroid tumours in various age groups of patients.
- ❑ To study the sex distribution of the Thyroid Neoplastic lesions.
- ❑ To appreciate the common symptomatology encountered in patients with thyroid neoplasms.
- ❑ To study the local examination findings suggestive of malignant Thyroid tumours.
- ❑ To find out the common histologic types of benign and malignant Thyroid tumours and calculate their frequency.
- ❑ To calculate the sensitivity of FINE NEEDLE ASPIRATION CYTOLOGY in different types of thyroid neoplasms.
- ❑ To calculate the percentage of false negative reports in FNAC.

## **MATERIALS AND METHODS**

This is a study of cases of thyroid neoplasms diagnosed and treated at Thanjavur Medical College Hospital during a period of 2 years & 2 months that is from January 2004 to February 2006. It is both a prospective and a retrospective study. All the histopathologically proven cases of benign and malignant thyroid tumours are included in the study.

A thorough history taking and a detailed clinical examination was made in all the cases [Proforma enclosed].

FINE NEEDLE ASPIRATION CYTOLOGY was done as a first line investigation in all these cases. Fine needle aspiration was done by the pathologists as per standard guidelines recommended by Svante. r.Orell.a minimum of 3 aspirations were done, usually with 25 gauge needle. The smears were fixed in isopropyl alcohol and were stained with routine haematoxylin and eosin stains, in a few cases giemsa stains was also used. Apart from basic hematological and radiological investigations [Xrays chest & neck], thyroid profile, IDL examination for vocal cord status and other investigations were done before operating on these patients.



The surgical treatment was offered upon the basis of clinical impression and FNAC results mainly. In a few patients even if the FNAC was towards a non neoplastic lesion, surgery was done based upon the clinical suspicion of malignancy.

The specimens were fixed with 10% buffered neutral formalin and sent to the pathologist. Apart from gross macroscopic examination and cut section examination, the histopathological examination was made by taking atleast 5 sections and processed. 3-5  $\mu$  thickness sections were cut and stained with haematoxylin and eosin. All these specimens were subjected to the histopathological examination and results obtained.

This study is directed towards the clinical presentation, the sensitivity of FNAC results and the percentage of false negative FNAC results in the histopathologically proved cases of Thyroid neoplasms.

## **REVIEW OF LITERATURE**

### **ANATOMY OF THE THYROID GLAND**

The thyroid gland consists of two symmetrical lobes united in the front of the second, third & fourth tracheal rings by an isthmus of glandular tissue. Apart from its thin capsule an envelope of pretracheal fascia encloses it.

Each lobe is pear shaped with a narrow upper pole and broader lower pole & appears approximately triangular on cross section with, lateral, medial, posterior surfaces. Lateral surface is under cover of sternohyoid and sternothyroid. The lower end of sternocleidomastoid overlaps these strap muscles. Medial surface lies against the lateral side of the larynx and upper trachea, and the part of oesophagus lies immediately behind. Posterior surface overlaps medial part of the carotid sheath. The Parathyroid glands lie in contact with this surface between it and fascial sheath. The isthmus joins the anterior surface of the lobes, towards their lower poles. The posterior surface of the isthmus is firmly adherent to the 2<sup>nd</sup>, 3<sup>rd</sup>, and 4<sup>th</sup>

tracheal rings and the pretracheal fascia is here fixed between them, it is called as ligament of berry. This is responsible for movement of the thyroid gland with deglutition.

A small portion of the gland substance often projects upward from the isthmus generally to the left of the midline as the pyramidal lobe and represents a development of glandular tissue from the caudal end of the thyroglossal duct. It is attached to the inferior border of the hyoid bone by fibrous tissue. Muscles fibres sometimes present in it, named as levator glandulae thyroideae and are innervated by a branch of the external laryngeal nerve. Separate masses of thyroid tissue (accessory thyroid glands) are not uncommonly found near the hyoid bone, in the tongue, in the superior mediastinum, beneath the sternocleidomastoid muscles.

### **Recurrent laryngeal nerve**

The right and left recurrent laryngeal nerves are intimately related to thyroid. The right one branches from the vagus as it crosses anterior to right subclavian artery. it loops around subclavian artery from posterior to anterior, crosses behind the right common carotid and ascends in or near the tracheoesophageal groove. It passes posterior to right lobe of thyroid to enter larynx.

The left nerve arises where the vagus crosses the aortic arch, just distal to origin of left subclavian artery from the aortic arch. it loops under the ligamentum arteriosum and the aorta, and ascends in the same manner as the right nerve. both nerves cross the inferior thyroid arteries near the lower border of the middle third of the gland. but variations in the courses can occur.

### **Superior laryngeal nerve**

This arises from the vagus and passes inferiorly, medial to the carotid artery. At the level of superior cornu of hyoid it divides into large, sensory, internal laryngeal nerve providing sensation to the larynx and a smaller, motor, external laryngeal nerve, serving the cricothyroid muscle.

### **External laryngeal nerve**

This is smaller and much less important than recurrent laryngeal nerve. It runs together with the superior thyroid vessels and then supplies cricothyroid and in its course lies a millimeter or two behind the superior thyroid artery passing medial to the upper pole.

### **Blood supply**

The thyroid gland is supplied by the superior thyroid artery, the first branch from the anterior aspect of the external carotid artery and the

inferior thyroid artery a branch from thyrocervical trunk. The thyroidea ima artery enters the lower part of isthmus in 3% of individuals. It springs from the brachiocephalic trunk.

Venous return is through the superior thyroid and middle thyroid veins, these enter into the internal jugular vein and through the inferior thyroid vein which enters brachiocephalic trunk.

### **Lymphatic drainage**

According to Hollinshead, the pattern of lymphatic drainage is as follows: the median superior drainage is by the digastric and prelaryngeal nodes. The median inferior drainage is by the pretracheal and the brachiocephalic nodes. The right and left lateral aspect drains into the lymph nodes of internal jugular chain. The posterior drainage is into the nodes along the recurrent laryngeal nerve and occasionally the retropharyngeal nodes.

### **Nerve supply**

The bulk of the sympathetic supply (vasoconstrictor) is derived from the middle cervical ganglion and enters the gland on the inferior thyroid artery. Some fibres are derived from the superior and inferior cervical ganglia. The vagal filaments are traceable to the gland but their purpose is unknown.

## **AETIOLOGY OF THYROID TUMOURS**

The exact aetiology of malignancy is unknown but may be related to

1. Low dose irradiation of the thyroid gland causes well-differentiated papillary cancer with multicentricity and Thyroid nodules.
2. Incidence of follicular carcinoma is more in endemic goitrous areas possibly due to TSH stimulation. Iodine abundance is associated with papillary cancer.
3. Malignant lymphomas sometimes develop in autoimmune thyroiditis so that the lymphatic infiltration in the autoimmune process may be an aetiological factor.
4. Activation of RET/D 10 S 170 fusion gene on chromosomes 10q 11-q12 and 1q32-q41 is specific for papillary carcinoma.

5. Increased expression of C –mys, C-fos, C-ras and C-erbB2/new has been reported in papillary thyroid cancer.
6. Inactivation of tumour suppressor gene on 3p facilitates the progression of follicular adenoma to follicular carcinoma.
7. The defect in Familial medullary carcinoma appears to be near the centromere of chromosome 10. Although these various associations have been described consistently the proof of causes and effect does not exist. Most thyroid gland tumours remain unassociated with obvious aetiological factors.

## **PATHOLOGY AND CLINICAL FEATURES OF THYROID TUMOURS**

The large majority of clinically apparent thyroid neoplasms are primary and epithelial. Traditionally they have been divided into adenomas and carcinomas together with the more common lesions composed of follicular cell.

From a histogenic standpoint it is preferable to divide the thyroid neoplasms into three major categories, depending on the cell types involved and subdivided them into various benign and malignant category.

1. Tumour exhibiting follicular differentiation.
2. Tumours exhibiting C-Cell differentiation
3. Tumours exhibiting follicular and C-cell differentiation.

Lesions in the first category comprises well over 95% of the cases.

Almost remainders are made up by tumours in the second category.



## **FOLLICULAR ADENOMA**

A benign encapsulated tumour composed of follicular cells.

Follicular adenoma occurs mostly in adults aged 20 – 50 years, but no age group is exempt. It is more common in females (male/female ratio 1 : 6)

Most present with a solitary thyroid nodule. Most patients are euthyroid adults who presented with the thyroid lump which on scan is usually “Cold”.

Many patients with adenoma have elevated thyroglobulin level but few are associated with hyperthyroidism. So called toxic adenoma.

It possesses the following characters.

1. Usually solitary surrounded by a grossly and microscopically complete capsule.
2. Exhibits variety of pattern singly or in combination.
  - ❑ Normofollicular (simple)
  - ❑ Macrofollicular (colloid)
  - ❑ Microfollicular (fetal)
  - ❑ Trabecular or solid (embryonal)
3. Mitoses are rare or absent in the follicular adenoma.
4. Secondary degenerative changes such as haemorrhage and cystic degeneration, bone formation, calcification, fibrosis, oedema are common.

Encapsulated thyroid tumours with a papillary pattern of growth are

- ❑ Hyperplastic nodule,
- ❑ Adenoma with papilloid formation
- ❑ Encapsulated papillary carcinoma.

### **Variants of Follicular Adenoma**

#### **Hurthle cell adenoma**

It composed of hurthle cells and lacking evidence of vascular and capsular invasion.

#### **Atypical adenoma**

Adenomas with pronounced cellular proliferation and less regular cytoarchitectural pattern but lacking evidence of capsular or blood vessel invasion.

#### **Hyalinizing Trabecular Adenoma**

Adenoma exhibiting prominent trabecular arrangement and equally prominent stromal hyalinization. The trabeculae may be straight or

curved resulting in an organoid formation. Occasionally nuclear grooves and psammoma bodies may be seen

### **Adenoma with bizarre Nuclei**

This is characterized by the presence of huge hyperchromatic nuclei usually in clusters, unaccompanied by other features of malignancy.

### **Other Rare Types**

Follicular adenoma with clear cell changes including signet ring, mucin producing and lipid rich types. Adenomas with adipose metaplasia of stroma – so called Adenolipoms.

## **PAPILLARY CARCINOMA**

Papillary carcinoma is defined by WHO as a malignant epithelial tumor showing evidence of follicular differentiation, typically with papillary and follicular structures as well as characteristic nuclear changes. This is the most common type of malignancy. Females are most commonly affected. It can affect any age group. The mean age at diagnosis being 43 years.

Most patients present with a painless neck mass. However some present initially with lymph node metastasis. Irradiation to the head and neck is a hazard. Some familial case with autosomal dominant inheritance have been reported, so-called familial non-medullary thyroid carcinoma.

### **PATHOLOGICAL FEATURES**

#### **Gross appearance :**

- ❑ Size of the primary tumour ranges from microscopic to huge.
- ❑ Most cases are solid, whitish, firm and clearly invasive.
- ❑ A complete capsule surrounds less than 10%.
- ❑ Marked cystic changes are seen in about 10% of cases.
- ❑ Sometimes papillary formations are evident on naked eye.

## **Microscopy**

Diagnosis of papillary carcinoma depends on the presence of certain architectural changes and / or characteristic nuclear changes.

- ❑ These are mainly in the form of true papillae.
- ❑ These papillae are usually complex, branching and randomly oriented with a central fibrovascular core and a single or stratified lining of cuboidal cells.
- ❑ Stroma of the papillae may be edematous or hyalinised and it contains lymphocytes, foamy macrophages, hemosiderin or exceptionally adipose tissue.
- ❑ The papillae are associated with formation of follicles.

## **Nuclear features**

- ❑ Ground glass optically clear nuclei.
- ❑ Nuclear pseudoinclusions
- ❑ Nucleus is usually inconspicuous
- ❑ Nuclear Grooves
- ❑ Psammoma bodies are seen in half of the cases. They are nearly synonymous with the diagnosis of papillary carcinoma.

- ❑ Lymphocytic infiltration seen in some cases.

## **VARIANTS OF THE PAPILLARY CARCINOMA**

- ❑ Papillary Microcarcinoma
- ❑ Encapsulated variant
- ❑ Follicular Variant
- ❑ Diffuse Sclerosing Variant
- ❑ Oxyphilic Variant
- ❑ Papillary carcinoma composed of hurthle cells
- ❑ Tall cell variant and columnar cell variant

## **FOLLICULAR CARCINOMA**

It is defined in a generic sense as any malignant thyroid tumour exhibiting evidence of follicular cell differentiation. It is a rare tumour, common in females in fifth decade. The incidence is higher in areas of endemic goiter, with iodine deficiency.

The most patients present with a thyroid mass, but up to 11% present initially with distant metastasis, the main mode of spread is hematogenous (predilection sites being bone and lung) rather than lymphatic.

Formed follicle to a predominantly solid growth pattern is seen. The diagnosis of carcinoma depends largely on the identification of capsular and / or blood vessel invasion. Accordingly the two types are

1. Minimally invasive follicular carcinoma
2. Widely invasive follicular carcinoma.

### **MINIMALLY INVASIVE FOLLICULAR CARCINOMA**

Grossly encapsulated tumour with solid and fleshy cut surface. Microscopy reveals following features : capsule of the follicular carcinoma tends to be thicker and more irregular than that of adenoma. Capsular invasion should be full thickness in order for the process to qualify as capsular invasion. Vessels should be of venous caliber and it should be

located in or immediately outside the capsule and it contain a cluster of tumour cells attached to the wall and protruding into the lumen.

### **WIDELY INVASIVE TYPE**

If often lacks encapsulation altogether. It shows wide spread infiltration of the blood vessels and/or adjacent thyroid tissue and both types are usually solitary, never occult, metastases through blood vessels.

### **HURTHLE CELL TUMOURS**

In this category are those tumours in which more than half of the cell population is made up of Hurthle cells. This is more common in adult females.

Tumours are solid, tan well vascularised and mostly well encapsulated. This invasive tumour tends to grow into parenchyma in a lobulated manner.

### **Microscopic**

Pattern of growth may be

1. Follicular
2. Trabecular / Solid
3. Papillary the most common.

The follicles are large and separated by thin fibrovascular septa that simulate papillae when cut tangentially. Presence of intraluminal colloid



with concentric laminations, having appearance strongly reminiscent of psammoma bodies. Nuclei show pleomorphism and prominent nucleoli. Benign form is known as hurthle cell adenoma. Tumour with clearcut evidence of capsular and/or blood vessel invasion are called hurthle cell carcinoma. It is an aggressive neoplasm.

### **POORLY DIFFERENTIATED CARCINOMA**

Patients with insular carcinoma are usually middle or old aged, with a mean age of 53 – 58.4 years. Women are more commonly affected than men (M : F = 1 : 2). The patients present with a thyroid mass. Rare patients present with bone metastasis. The disease is often locally advanced at presentation. Lymph node and distant metastases are possible.

#### **Microscopy**

Microscopic examination reveals nesting pattern of growth solid to microfollicular arrangements small uniform tumour cells with variable mitotic activity and fresh tumour necrosis.

### **ANAPLASTIC (UNDIFFERENTIATED) CARCINOMA**

Anaplastic carcinoma comprises 3 – 5 % of all thyroid carcinomas. Endemic goiter and radiation are possible etiologic factors. Male/Female ratio is 1 : 1.1 to 1 : 1.4 and mean age is 66.6 years.

The disease is usually so widely invasive at presentation that it is inoperable in about half of the cases. Regional lymph node and distant metastases (mostly) to lungs, sometimes bones) are common.

Recent rapid enlargement of thyroid in a patient with long – standing goiter is the commonest presentation.

### **Microscopy**

Three major patterns occur, sometimes in combination. They are squamoid cells, spindle cell, giant cell patterns.

The exhibit fascicular or storiform pattern of growth, heavy neutrophilic infiltration, prominent vascularization and metaplasia. Nearly all sarcoma like tumours are in reality, undifferentiated carcinomas. Common and diagnostically useful features are palisading at the necrotic edges and tendency for the tumour cells to invade the wall of veins.

## **MEDULLARY CARCINOMA OF THYROID**

It is a medullary thyroid carcinoma is a malignant tumour showing parafollicular C – cell differentiation. It characteristically secretes calcitonin.

Most patients present with a thyroid mass, pain, dysphagia, hoarseness or cervical lymphadenopathy. About 20-40% of patient have diarrhea. Cushing syndrome results from ACTH secretion. Approximately 70 – 80% of medullary carcinomas are sporadic, and most such tumors are unilateral. The hereditary variety (autosomal dominant with high penetrance and variable expression) accounts for 20-30% of cases. In the latter setting, the tumor often develops at an earlier age, multicentrically and bilaterally, and on a background of C – cell hyperplasia. The hereditary forms of medullary carcinoma are caused by germline mutation in the *RET* gene.

### **Microscopy**

Solid proliferation of round to polygonal cells of granular amphophilic cytoplasm and medium sized nucleus separated by highly vascular stroma, hyalinized collagen and amyloid coarse calcification is common.

### **Variants**

- 1, Inflammatory type
- 2, So – called anaplastic type

3, Mucinous medullary carcinoma

4, Clear cell variant

5, Small cell type

6, Pigmented variant

7, True papillary form

## **MALIGNANT LYMPHOMA**

Primary lymphoma of the thyroid is uncommon comprising only approximately 2.5 – 3% of all extranodal lymphomas. Thyroid lymphoma occurs more commonly in females (M : F = 1 : 2.45) usually in middle to old age (59 – 68 Years). The lymphomas commonly arise in a setting of Hashimoto thyroiditis or lymphocytic thyroiditis.

Lymphoma forms a non-circumscribed rubbery to soft. In microscopy diffuse large B-cell lymphoma (>50%) and extranodal marginal zone B-cell lymphoma of MALT type account for almost all cases.

## **THYROID NODULE WITH RISK FACTORS FOR MALIGNANCY**

- ❑ Age <20 or >60 years
- ❑ History of neck irradiation
- ❑ Male sex
- ❑ Femaly history of medullary cancer
- ❑ Rapid growth
- ❑ Hoarsenss of voice
- ❑ Firm and hard, non tender nodule
- ❑ Regional Lymphadenopathy
- ❑ Fixation to adjacent tissue
- ❑ Vocal Cord paralysis

## **HISTORICAL DEVELOPMENT of FNA CYTOLOGY**

It was in 1904, when **Greig and Gray** aspirated a lymphnode to diagnose Trypanosomiasis, the clinical use of aspiration cytology was introduced for the first time in the history. Fine needle aspiration cytology has been used in Sweden since 1950. It does not supplement histology but augments it.

In 1858, **Rudolf Virchow**, published his cellular physiology  
**Ward** in 1912, used FNAC to examine lymphnode for lymphoma.

**Guthrie** in 1921 firs used lymphnode aspiration on a systematic basis.

In 1957 **Gibson and Smith** published their report on FNAC. At the Radiumhemmet in Stockhom about 12000 aspirations were performed every year, 2000 on thyroid alone. Other centers using this technique on a

large scale are the “**Harzen Institute of Oncology**” in Moscow and the **Curie foundation at Paris**.

A current authoritative view on FNAC of thyroid Neoplasm has been published by Lowhagen et al 1979 and Chu et al 1979.

Of the many workers it was **Johannes Muller** who set the foundation of clinical cytology. In 1938 he published on the nature and structural characteristic of cancer and those morbid growth that may be confended with it.

Presently FNAC is routinely done in may centers also in India. With further advance, the accuracy rate has been increased with the analysis of DNA content of the aspirates and correlation of cytology examination with DNA analysis. (**Atkin N.B: Br. J. Cancer 40 : 210-221, 1979**).

## **INVESTIGATIONS**

### **FINE NEEDLE ASPIRATION CYTOLOGY**

It is the first line basic investigation after clinical examination. FNAC can diagnose most of the thyroid neoplastic lesions but it cannot confidently differentiate follicular adenoma and follicular carcinoma. because the capsular and vascular invasion of a follicular carcinoma cannot be made out with FNA cytology.



## **FOLLICULAR NEOPLASM**

Criteria for diagnosis:

Cellular ,often bloody smear

Many equal sized epithelial clusters scattered throughout smear

Syncytial cell aggregates, nuclear crowding and overlapping.

Microfollicles and rosettes.

**Scanty or no colloid**

Problems in diagnosis:

Nodular goitre, vascularity, papillary carcinoma, atypical, parathyroid adenomas, cystic change, inspissated colloid.

## **INSULAR CARCINOMA**

Criteria for diagnosis:

Cellular smears

Cells in clusters , no architectural pattern

No colloid

Problems in diagnosis

Other neoplasms, metastasis

## **PAPILLARY CARCINOMA**

## **Criteria for diagnosis**

Cellular smears

Syncytial aggregates, distinct borders, nuclear crowding and overlapping.

Papillary fragments.

Enlarged ,ovoid, pale nuclei, powdery chromatin.

Multiple nucleoli, intracytoplasmic inclusions, nuclear grooves.

Dense cytoplasm

Chewing gum colloid

Psammoma bodies.

## **Problems in diagnosis**

Cystic change, lymphocytic infiltration, papillary adenoma, hyalinising trabecular adenoma, crystals, inspissated colloid.

## **MEDULLARY CARCINOMA**

### **Criteria for diagnosis**

Cellular smears, some syncytial aggregates

Variable cell pattern

Moderate anisokaryosis

Nuclear chromasia

Cells with red cytoplasmic granularity

Amyloid

Positive staining for calcitonin

Problems in diagnosis

Variants of medullary ca follicular neoplasms, Oxyphilic cell neoplasms

Paragangliomas

## **ANAPLASTIC CARCINOMA**

Criteria for diagnosis

Bizarre, large malignant cells-epithelial or spindle or rarely undifferentiated cells

Marked nuclear pleomorphism, multinucleation, mitosis.

Necrotic cells.

Problems in diagnosis

Background of fibrosis or inflammatory reaction, fibroblastic or histiocytic cells

Variants of anaplastic ca, metastasis.

## **LYMPHOMA**

Most are of B cell lineage and MALT type, including low or high grade forms.

Majority are associated with hashimotos thyroiditis and difficult to differentiate.

Problems in diagnosis

Autoimmune thyroiditis, small cell anaplastic ca.

## **CORE NEEDLE BIOPSY**

This can be done in large, hard, fixed neck mass frequently on a basis of anaplastic ca and lymphoma.

Complications: bleeding, nerve injury, tracheal perforation, tumor implantation.

## **RADIOIODINE SCANS**

I -131, I-123 and pertechnetate can be used.

It may suggest a cold, warm, hot nodule. It cannot differentiate benign and malignant nodules. Although most thyroid carcinomas are cold, they constitute only 14-22% of nonfunctioning nodules.

### **THYROID FUNCTION TESTS**

The estimation of T3, T4, TSH establishes the functional status of the gland. Most of the patients with neoplasms do not have an altered function.

### **ULTRASONOGRAPHY**

It can find out the size, number of nodules and determine whether the nodule is solid or cystic.

A solid mass is mostly benign, but has the highest chances of being malignant. Conversely, a cystic mass is not always benign but it has higher likelihood of being benign than a solid one.

A halo sign is a thin sonolucent rim that supposedly occurs around benign tumors, but may be observed in a few carcinomas.

Doppler ultrasound assesses the vascularity of the gland and the infiltration of the carotid artery by the carcinomas.

Lymph node metastasis can be detected.

It is a safe, flexible, observer dependent investigation that has a role in follow up.

### **CT SCAN AND MRI**

These investigations are useful in selected patients to define the anatomical extent of the tumor, retrosternal extension of the thyroid. Lymph node metastasis can be detected in cases of malignancies.

### ***STANDARD RADIOGRAPHY***

A chest x-ray and neck x-rays may be useful in presence of obstructive symptoms, tracheal deviation, retrosternal extension and in case of pulmonary metastasis. Calcifications can rarely be made out.

### **INDIRECT LARYNGOSCOPY**

IDL can find out the vocal cord paralysis due to involvement of recurrent laryngeal nerve by the tumor. It is done routinely before surgery during preoperative evaluation.

### **TUMOUR MARKERS**

Serum thyroglobulin level is used as a marker in follow up of patients with differentiated thyroid cancers. Normal range:1-35 micrograms per litre.

Serum calcitonin is used as a marker in patients with medullary ca. Normal Being less than 0.08 micrograms per litre.

## **TREATMENT OF THYROID NEOPLASMS**

### **Follicular Adenoma**

Follicular adenomas usually present as solitary nodule and there is no capsular/vascular invasion. Hence it is treated by LOBECTOMY.

### **Differentiated Thyroid CA :**

This includes the papillary and follicular carcinomas.

A conservative approach can be followed for the low risk group patients with unilateral involvement. It is by LOBECTOMY & ISTHUMECTOMY. At the same time, clinically obvious nodes are removed. If the jugular nodes are extensively involved, MODIFIED NECK DISECTION is indicated.

NEARTOTAL/TOTAL THYROIDECTOMY is indicated in all cases of high risk patients and patients with obvious bilateral disease at operation.



## **ADDITIONAL MEASURES**

### **Thyroxine**

It is a standard practice to give 0.1 – 0.2 mg thyroxine daily to all operated patients on the basis that differentiated thyroid cancer is TSH dependent.

Thyroxine replacement is obvious in patients treated with total thyroidectomy.

### **Radio Iodine**

If metastasis take up radioiodine, they may be detected by scanning and treated with large doses of radioiodine.

Solitary distant metastasis may be treated by external radiotherapy.

## **ANAPLASTIC CARCINOMA**

In a minority of patients, if the disease appears confined to thyroid and possibly strap muscles, complete resection is justified.

Some present with tracheal obstruction, requiring emergency ISTHUMECTOMY.

Radiotherapy, a worthwhile palliation should be given in all cases.

### **MEDULLARY CARCINOMA**

It is treated by TOTAL THYROIDECTOMY and resection of involved lymph nodes by radical or modified radical neck dissection.

Familial cases are now detected by screening for RET mutations. Prophylactic surgery is now being recommended in infants with the genetic triad.

Before surgery, in all cases pheochromocytoma should be excluded.

### **MALIGNANT LYMPHOMA :**

Treatment is by radiotherapy and / or chemotherapy response to irradiation is good and radical surgery is unnecessary once diagnosed by biopsy. In patients with tracheal compression, isthumectomy is the appropriate biopsy.

## **OBSERVATION AND RESULTS**

The study covered 82 cases of Thyroid Neoplasms at Thanjavur Medical College Hospital during January 2004 to February 2006, a 2 years & 2 months period.

Among the total 82 Histopathologically proven cases, 49 cases were benign (59.75%) and 33 cases were malignant (40.25%).

All the 49 cases of benign thyroid neoplasms were follicular adenomas (including few of its variants). Among the 33 cases of malignancies, 30 were papillary carcinoma, 1 was follicular carcinoma, 1 was medullary carcinoma and 1 was anaplastic carcinoma.

## **AGE DISTRIBUTION**

The cases were grouped into specific age groups as follows: those below 20 years, 21 – 30 years, 31 – 40 years, 41-50 years, 51-50 years and those above 60 years.

The age distribution of the patients with thyroid neoplasms are as follows

| <b>Age Group<br/>(Years)</b> | <b>Males</b> | <b>Females</b> | <b>Total</b> | <b>% of Cases</b> |
|------------------------------|--------------|----------------|--------------|-------------------|
| ≤ 20                         | 1            | 1              | 2            | 2.4%              |
| 21 – 30                      | 2            | 22             | 24           | 29.3%             |
| 31 – 40                      | 1            | 23             | 24           | 29.3%             |
| 41 – 50                      | 4            | 18             | 22           | 26.8%             |
| 51 – 60                      | 2            | 6              | 8            | 9.8%              |
| > 60                         | 0            | 2              | 2            | 2.4%              |

Among the 49 cases of **Follicular Adenoma**, the youngest patient was 19 years old and the eldest patient was 60 years old. The **Mean Age** was 38.59 years.

Among the 30 cases of **Papillary Carcinoma**, the youngest was 18 years old and the eldest patient was 70 years old. The **Mean Age** for papillary carcinoma was 39.83 years.

1 case of **Follicular Carcinoma** was a 30 year old female.

1 case of **Medullary Carcinoma** was a 39 year old female.

1 case **Anaplastic Carcinoma** a 55 year old female.

The age distribution for benign tumors is as follows:

### **BENIGN TUMOURS**

| <b>Age Groups<br/>[years]</b> | <b>No. of cases</b> | <b>% Of cases</b> | <b>Mean age:<br/>38.59 years</b><br><br><b>Age range<br/>19 to 60 years</b> |
|-------------------------------|---------------------|-------------------|---|
| ≤ 20                          | 1                   | 2.04%             |   |
| 21-30                         | 15                  | 30.61%            |   |
| 31-40                         | 12                  | 24.49%            |   |
| 41-50                         | 16                  | 32.65%            |   |
| 51-60                         | 5                   | 10.20%            |   |
| >60                           | 0                   | 0.00%             |   |

Distribution Of Malignant Tumors is as follows:

### **MALIGNANT TUMOURS**

| <b>Age Groups<br/>[years]</b> | <b>No. of cases</b> | <b>% Of cases</b> | <b>Mean age:<br/>39.97 years</b> |
|-------------------------------|---------------------|-------------------|----------------------------------|
| ≤ 20                          | 1                   | 3.03%             |                                  |

|       |    |        |                                     |
|-------|----|--------|-------------------------------------|
| 21-30 | 9  | 27.27% | <b>Age range<br/>18 to 70 years</b> |
| 31-40 | 11 | 33.22% |                                     |
| 41-50 | 5  | 15.15% |                                     |
| 51-60 | 5  | 15.15% |                                     |
| >60   | 2  | 6.06%  |                                     |

### **SEX DISTRIBUTION**

Among the total 82 cases, 67 were females (81.71%) and 15 were males (18.29%).

The sex distribution for both benign and malignant tumors are as follow:

| <b>Tumors</b> | <b>Total</b> | <b>Males</b> | <b>Females</b> |
|---------------|--------------|--------------|----------------|
| Benign        | 49           | 9 (18.37%)   | 40 (81.63%)    |
| Malignant     | 33           | 6 (18.18%)   | 27 (81.81%)    |

So, the sex ratio for Thyroid Neoplasms are as follows :

Benign tumours

Male : Female = 1 : 4.4

Malignant tumours

Male : Female = 1 : 4.5

### **FREQUENCY OF HISTOLOGICAL TYPES OF TUMOURS :**

Among the 82 cases, 49 were benign and all of them were follicular adenomas and its variants.

33 Cases of malignancy comprises of,

30 Papillary carcinomas

1 Follicular carcinoma

1 Medullary carcinoma

1 Anaplastic carcinoma

| <b>Tumors</b> | <b>No. of cases</b> | <b>Percentage</b> |
|---------------|---------------------|-------------------|
| Benign        | 49                  | 59.75             |
| Malignant     | 33                  | 40.25             |

Among malignant tumors the histological types were as follows :

| <b>Tumors</b>        | <b>No. of cases</b> | <b>Percentage</b> |
|----------------------|---------------------|-------------------|
| Papillary carcinoma  | 30                  | 90.91             |
| Follicular carcinoma | 1                   | 3.03              |
| Medullary carcinoma  | 1                   | 3.03              |
| Anaplastic carcinoma | 1                   | 3.03              |

#### **SYMPTOMATOLOGY :**

Thyroid enlargement was the most common presentation of the neoplasms of thyroid gland.

Most of the patients presented with a painless swelling in the neck. Obstructive symptoms were rarely encountered among which hoarseness was even rarer when compared to dyspnea and dysphagia.

| <b>Tumors</b>     | <b>No. of Patients</b> | <b>Percentage</b> |
|-------------------|------------------------|-------------------|
| Painless swelling | 72                     | 87.8              |



|                     |    |       |
|---------------------|----|-------|
| Painful swelling    | 10 | 12.20 |
| Dysphagia           | 7  | 8.54  |
| Dyspnea             | 6  | 7.32  |
| Hoarseness of voice | 5  | 6.98  |

## **SIGNS IN MALIGNANCY :**

The reliable clinical findings suspicious for malignancy are the firm/hard consistency, fixity to surrounding structures and cervical lymphadenopathy. They were distributed as follows :

Table 1

| <b>Consistency</b> | <b>No.of patients</b> |
|--------------------|-----------------------|
| Soft               | 1                     |
| Firm               | 29                    |
| Hard               | 2                     |

Table 2

| <b>FIXTY</b> | <b>No.of patients</b> |
|--------------|-----------------------|
| Yes          | 4                     |
| No           | 29                    |

Table 3

| <b>LYMPHNODE<br/>ENLARGEMENT</b> | <b>No. of patients</b> |
|----------------------------------|------------------------|
| Yes                              | 9                      |

|    |    |
|----|----|
| No | 24 |
|----|----|

## SENSITIVITY OF FNAC

Sensitivity is the ability of a test (here, FNAC), to identify correctly all those who have the disease, (here, HPE proven cases of thyroid neoplasms) that is “true positive”.

“True positives” are those individuals found positive on the test (here, FNAC) who have the condition or disorder being studied.

“False negatives” include those with negative test (here, FNAC) results who have the disease.

**No. of true positive**

**Hence, sensitivity =** \_\_\_\_\_

**No. of true positive + No.of false negative**

In this study,

Total No.of true positive FNAC = 70

[i.e. Both FNAC and HPE positive cases]

Total No.of False negative FNAC = 12

[i.e. FNAC negative and HPE positive cases]

So, FNAC sensitivity for Thyroid Neoplasms in this study is

$$\frac{70}{70+12} \times 100 = \mathbf{85.37\%}$$

Sensitivity for various Thyroid Neoplasms :

| <b>Type of Tumour</b>                 | <b>True<br/>Positive</b> | <b>False<br/>Negative</b> | <b>Sensitivity</b> |
|---------------------------------------|--------------------------|---------------------------|--------------------|
| Follicular Neoplasm                   | 40                       | 10                        | 80 %               |
| Papillary carcinoma                   | 28                       | 2                         | 93.33%             |
| Medullary carcinoma<br>(1 case only)  | 1                        | 0                         | 100%               |
| Anaplastic carcinoma<br>(1 case only) | 1                        | 0                         | 100%               |

## PERCENTAGE OF FALSE NEGATIVE FNAC REPORTS

False negatives” include those with negative test (here, FNAC) results who have the disease.

$$\text{Percentage of false negatives} = \frac{\text{No. of False Negatives}}{\text{No. of true positive} + \text{No. of false negative}}$$

In this study,

Percentage of False Negative FNAC for Thyroid neoplasms (i.e., percentage of FNAC negative and HPE Positive cases)

$$\frac{12}{70+12} \times 100 = \mathbf{14.63\%}$$

Sensitivity for various Thyroid Neoplasms :

| Type of Tumour      | False Negative | True Positive | % of False Negatives |
|---------------------|----------------|---------------|----------------------|
| Follicular Neoplasm | 10             | 40            | 20%                  |

|                                       |   |    |       |
|---------------------------------------|---|----|-------|
| Papillary carcinoma                   | 2 | 28 | 6.66% |
| Medullary carcinoma<br>(1 case only)  | 0 | 1  | 0%    |
| Anaplastic carcinoma<br>(1 case only) | 0 | 0  | 0%    |

These were the observations and results of this study of Thyroid neoplasms at Thanjavur Medical College Hospital during the period of January 2004 to February 2006.

## **DISCUSSION**

In this study of thyroid neoplasms, findings on the clinical presentation reveal that the factors like age, sex, presenting symptoms, signs, type of tumors commonly encountered, etc coincides with that of available literature, although thyroid neoplasms are well known for its wide variations in their geographical distribution.

In this study of 82 cases of thyroid neoplasms, 70 cases were found to be true positive with a sensitivity of 85.37% and 12 cases were false negative. The false negatives are mainly due to the following reasons.

- Aspiration not striking the representative area
- Inadequate aspiration
- Failure in producing acceptable smears
- Faulty fixation
- Geographic misses or dual pathology
- Error in interpretation

## **INTERNATIONAL LITERATURE**

### **Ashcroft And Van Henle And By Frable**

In the reviews of **Ashcroft and van Henle and by Frable**, FNAC is shown to achieve a diagnostic accuracy of over 90% in terms of predictive value, sensitivity, specificity and efficiency in the diagnosis of neoplasm and this has been confirmed in a number of recent studies.

### **Ackerman and Silverman et al**

**Ackerman and Silverman et al** have claimed a sensitivity and specificity of over 90% & have recommended FNAC as the initial test in the evaluation of any thyroid nodule.

The reported false positive rate is usually low, being around 1-2% of the total number of malignancies. In some highly experienced centers the false positive rate approaches to zero by **Ackerman et al** and the cytological report can be used as basis for definitive surgery.

**Anderson Webb 1987, Klemi et al 1991, La Rosa et al 1991**

Accumulated experience with FNAC and cytology to date suggested that the incidence of false positive diagnosis of malignancy is extremely low (**Anderson & Webb 1987**). Of greater concern is the potential for false negative diagnosis, which in earlier series ranged from 6 to 27% (Granberg et al 1983) Subsequent publication suggested that the false negative rate can be maintained at the lower end of spectrum (**Anderson Webb 1987, Klemi et al 1991, La Rosa et al 1991**).

To avoid misdiagnosis of carcinoma of the thyroid resection should be advised after fine needle aspiration and cytology in the following circumstances.

- ❑ All proven malignant nodules
- ❑ All cytologically diagnosed follicular neoplasm
- ❑ All lesions exhibiting an atypical non-diagnostic cellular pattern on cytology.
- ❑ Cystic nodules which recur following aspiration



When, on clinical grounds, the index of suspicion of malignancy is high, even if the cytology report suggested benign disease.

**Rosen et al 1981, Hamberger et al 1982, Franklyn & Sheppard 1987, Wheeler 1988**

Despite its limitations, there can no longer be any doubt that FNAC now represents the prime investigation in the assessment of the patient with thyroid nodule and should be employed routinely (**Rosen et al 1981, Hamberger et al 1982, Franklyn & Sheppard 1987, Wheeler 1988**).

## CONCLUSIONS

This study on Thyroid neoplasms at Thanjavur Medical College for a period of 2 years and 2 months from January 2004 – February 2006 has led to the following conclusions.

- About 59.75% of **thyroid neoplasms** operated were found to be benign and the remaining 40.25% malignant.
- **Follicular adenoma** is the commonest type among follicular neoplasms and also the commonest benign thyroid neoplasm.
- **Papillary carcinoma** is the most common type of thyroid malignancy.
- Both benign and malignant thyroid tumors are more frequent in females. Sex ratio for benign tumours is (Male : Female) **1 : 4.4** for malignancy it is **1 : 4.5**.
- About 95.2% of the neoplasms were encountered in **20 – 60 years** age group.
- Benign tumours are common in the third and fourth decade, with a mean age of **38.59 years**.

- Malignant tumors are common in third and fourth decade with mean age of **39.83 years**.
- **Painless neck swelling** was the commonest presenting symptom in thyroid tumors obstructive features & signs suggestive of malignancy like hard consistency, fixity, presence of lymph adenopathy, recurrent laryngeal nerve were encountered in relatively fewer cases.
- The **sensitivity of FNAC** in thyroid neoplasms is 85.37% with a sensitivity of 80% for follicular neoplasms and 93.33% for papillary carcinomas.
- The **% of false negative results** for Thyroid neoplasm was 14.63% with 20% for follicular neoplasm and 6.66% for papillary carcinoma.
- **FNAC** is a highly useful, simple, relatively non traumatic first line investigation tool for thyroid neoplastic lesions with good patient acceptance rate.

### **CLINICAL PROFORMA**

Name :  
 Age :  
 Sex :  
 In patient number :  
 Occupation :  
 Income :

**HISTORY:**

Onset of the swelling , its duration, rate of growth.

Sudden increase in size

Associated pain

Difficulty in swallowing or respiration

Hoarseness of voice

Symptoms suggestive of hypo or hyperthyroidism

Loss of weight and appetite

Irradiation history

Any other member in family affected

Treatment history

**GENERAL EXAMINATION****PHYSICAL EXAMINATION**

Vital signs:

Pulse rate, rhythm, character, volume, deficit.

Blood pressure

Respiratory rate

Temperature

**General appearance, signs suggestive of toxicosis**

**INSPECTION:**

Uniformity

Nodules- isolated or multiple, size, extent

Surface, borders

Lateral swellings

Movement with deglutition and protrusion of tongue

Pressure on great vessels

**PALPATION:**

Generalized enlargement or localized

Size, position,

Extent, borders

Surface

Consistency

Mobility

Pressure effects: kocher's test, carotid pulsation, sympathetic trunk

signs

Examination of cervical lymphnode enlargement

Examination for metastasis:

Bony: skull, spine, pelvis, long bones

Pulmonary metastasis.

Examination of other systems

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